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13. ABSTRACT (Maximum 200 Words)

This is a two-year randomized trial of the effects of oral contraceptives on bone mass and stress fractures incidence among 151 female competitive distance runners in the age range 18-25 years. The Coordinating Center is at Stanford University and bone mass is being measured at five sites: Massachusetts General Hospital, University of California Los Angeles, University of Michigan, Stanford University/Palo Alto VA Medical Center, and Helen Hayes Hospital in West Haverstraw, NY. Athletes were recruited mostly from the areas around these five clinical sites. Over the five clinical sites, 151 runners were randomized, and follow-up continues. Follow-up will be completed in October 2005, and final results of the study should be available in early 2006.

14. SUBJECT TERMS
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(5) INTRODUCTION

Highly trained female athletes may experience loss of menses because of their participation in intense physical activity. Previous cross-sectional research has shown that women with exercise-induced menstrual irregularities have a significantly higher frequency of stress fractures and low bone mass than normally menstruating controls. Longitudinal studies suggest that these women are losing bone mass over time. Low serum estrogen levels are believed to be a principal cause of the bone loss. If so, re-establishing normal estrogen levels in these women should prevent or retard bone loss and decrease the incidence of stress fracture. This study is a two-year randomized trial of the effect of oral contraceptives on bone mass and stress fracture incidence among 151 female cross country runners in the age range 18-25 years. The Coordinating Center is at Stanford University and bone mass is being measured at five sites: the Massachusetts General Hospital, the University of California Los Angeles, the University of Michigan, Stanford University/Palo Alto VA Medical Center, and the Helen Hayes Hospital in West Haverstraw, NY. Athletes are being recruited mostly from the areas around these five clinical sites.

(6) BODY

Below we summarize (a) our progress through year 6, and (b) our plans for completing the study.

(a) Progress through year 6:

As of the time of this writing (January 2005), of the 151 runners randomized; 95 have completed the study, of whom 77 had two follow-up visits and 18 only one follow-up visit. An additional 25 have had one follow-up visit and are on time to have a second follow-up visit before the study ends in October 2005. Another 5 have had one follow-up visit, but are delinquent for their second follow-up visit. Thus, at this time we have at least some follow-up bone mineral density

measurements on 125 (83%) of the 151 who were randomized. Of the remainder, 19 have either withdrawn or are lost to follow-up, and 7 may be lost, although we have not quite given up. During year 6 specifically, 25 attended their first follow-up visit, and 20 completed the study.

(b) Plans for completing the study: We expect to complete data collection by October 2005, and to have data analysis for the primary objectives completed by in early 2006.

(7) KEY RESEARCH ACCOMPLISHMENTS: During the past budget year we have concentrated on data collection rather than publications. However, below under Conclusions we report on some interesting interim results

(8) REPORTABLE OUTCOMES: None during the past year.

(9) CONCLUSIONS: We will have no firm conclusions to report on the primary hypothesis of the study until the end of the trial. However, we presented interim results to the U.S. Army Research Institute of Environmental Medicine in Natick, MA on June 8, 2004. At that time, at least partial follow-up data were available for 122 participants, and two-year follow-up data for 67 participants.

Our results concurred with previous findings that peak bone mineral density (BMD) in women is predominantly established by age 18. Among eumenorrheic women, the mean annual change in BMD was close to zero in both the treatment and control groups. Oligomenorrheic and amenorrheic women had small increases in spine BMD and total bone mineral content (BMC) that correlated strongly with increasing period regularity, but not with randomization to treatment. Baseline calcium intake predicted small increases in total bone mass and hip BMD.

Gains in fat mass predicted increases in spine BMD. Gains in lean mass predicted increases in hip BMD.

At the time of the interim analysis, 18 participants had sustained a total of 22 stress fractures during follow-up. Randomization to treatment was not significantly associated with stress fracture risk [hazard ratio: 0.82 (0.30-2.27)]. However, increasing duration of oral contraceptive use (ignoring intention-to-treat) was associated with a significant decrease in stress fracture risk. A history of stress fractures prior to enrollment in the study strongly predicted subsequent stress fracture risk, controlling for BMD at baseline. Low calcium intake and low BMC and BMD at baseline were also strong predictors of fracture risk in all menstrual groups.

(10) REFERENCES: None

(11) APPENDICES: None.